



PATENT
3920-0110P

IN THE U.S. PATENT AND TRADEMARK OFFICE

Applicant: John CARTER

Appl. No.: 10/089,846

Group: 1616

Filed: June 6, 2002

Examiner: Choi

For: PHARMACEUTICAL COMPOSITIONS AND THEIR
USE IN THE TREATMENT OF NEOPLASTIC DISEASE

DECLARATION UNDER 37 CFR 1.132
(#2)

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Roger Anthony Oakes, do hereby declare and state as follows:

1. I am Roger Anthony Oakes and am employed by Ivy Medical Chemicals Ltd., 54 Sun Street, Waltham Abbey, Essex, EN9 1EJ, UK, as Scientific Director.
2. I have read and am familiar with the specification and claims of the above-identified patent application.
3. In order to confirm the advantages of the invention described and claimed in the above application, the following studies were conducted under my supervision and control.

4. The study was conducted to assess the anti-tumor activity of the composition CV247 in connection with the effect of the composition on the growth of transplantable tumors in inbred mice.

5. The CV247 composition comprised the following components:

| | |
|---------------------|-------------------------|
| Sodium salicylate | 3.5 mg/mL |
| Ascorbic acid | 4.0 mg/mL |
| Copper gluconate | 0.2 mg/mL (0.028 mg Cu) |
| Manganese gluconate | 0.2 mg/mL (0.025 mg Mg) |

6. A total of 50 male C57B1/6 mice were each injected subcutaneously with 3×10^6 RMA lymphoma cells, a dose known to give 100% tumor "take". A total of 24 experimental mice were initially treated with 0.1 ml of CV247 having the above composition.

7. There was no significant difference between the experimental and control animals during the early time points, based on the size of the tumors in the respective groups of mice. However, a statistically significant difference in the size of tumors occurred when measured from day 17, as well as for the weight of the respective tumors. In addition, at day 17, 4 tumors were too small to measure in mice initially treated with CV247, compared with only 1 tumor in the control group. In a number of mice, more than 1 tumor grew along the injection needle tract. However, this occurrence was considerably more frequent in the control group of mice (having occurred in 10 mice) than in the group of mice having been treated with CV247 (having occurred in 1 mouse). Further, in 3 control mice, tumors could not be excised because they were infiltrating deeper

tissues. No side effects were observed with respect to the administration of CV247 in the treated group of mice.

8. The statistical results of the study are summarized below (tabulated mean data), which demonstrate that the administration of CV247 exhibits a measurable effect on the growth rate of RMA thymoma in mice:

| <u>Group</u> | <u>Size</u> (Day 13) | <u>Size</u> (Day 15) | <u>Size</u> (Day 17) | <u>Weight</u> (Day 17) |
|--------------|-------------------------|-------------------------|-------------------------|---------------------------|
| Control | 0.23 | 0.69 | 1.14 | 0.92 |
| Treated | 0.22 | 0.39 | 0.63 | 0.46 |

9. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dated: 18th JUN 2008

Signed: 